REMARKS

As a preliminary matter, applicants would like to thank Examiner Mojdeh Bahar for the courtesies extended during the Examiner Interview held at the Office on July 21, 2003.

With this amendment, claim 77 has been amended to include albuterol among the list of preferred short-acting bronchodilators. No other claim amendments are presented with this paper. As albuterol is recited in independent claim 51, it follows that no new matter is added to the application with the amendment to claim 77.

OUTLINE OF THE PROSECUTION HISTORY:

The present application was filed on August 1, 2001, with 74 claims.

On June 19, 2002, the Office mailed an Office Action requiring restriction of the claims between the following two groups:

Group I: drawn to a pharmaceutical formulation, a drug delivery system device, and a dosage form comprising a corticosteroid and a bronchodilator (claims 1-50 and 56-74); and

Group II: drawn to a method of treating pulmonary disease responsive to treatment with a bronchodilator/corticosteroid combination (claims 51-55).

The Office Action also required election of a single species of corticosteroids and a single species of bronchodilators. On July 19, 2002, a Preliminary Amendment and Response to Restriction Requirement was filed electing the method claims of Group II; amending claims 51-54; adding new claims 75-116; and electing anhydrous mometasone furoate as the corticosteroid and pirbuterol acetate as the bronchodilator.

On September 10, 2002, the Office mailed the first Office Action on the merits, which withdrew claims 80-83 as drawn to a non-elected species and examined and rejected claims 51-54, 75-79, and 84-116 under 35 U.S.C. § 103 as obvious over Sequeira et al. in view of the PDR monograph for the Maxair® inhaler ("Maxair monograph"). The response filed on January 10, 2003, amended claim 51 to further define the recited corticosteroid and the bronchodilator; canceled claim 77 and amended the dependency of claim 77; and presented arguments traversing the Examiner's obviousness rejection.

In the Office Action under reply, claims 51-55, 75, 77-79, and 84-116 have once again been rejected over Sequeira et al. in view of the Maxair monograph.

On July 21, 2003, an Examiner interview was held at the Office to discuss the merits of the invention. The arguments that follow and the attached Declaration of Leonard W. Kaplan under 37 C.F.R. § 1.132 ("Kaplan Declaration") address the Examiner's concerns with the claimed invention and demonstrate the nonobviousness of the claimed invention.

CLAIM REJECTIONS – 35 U.S.C. § 103(a)

Claims 51-55, 75, 77-79, and 84-116 stand rejected under 35 U.S.C. § 103(a) as obvious over Sequeira et al. in view of the Maxair monograph. This rejection is respectfully traversed.

When establishing a *prima facie* case of obviousness, the Office must show that the cited prior art references, either singly or in combination, suggest the desirability of the claimed subject matter. *In re Deminski,* 796 F.2d 436, 230 USPQ 313 (Fed. Cir. 1986). Factors including unexpected results, new features, solution of a different problem, and novel properties, are all considerations in the determination of obviousness under 35 U.S.C. § 103. *In re Rouffet,* 149 F.3d 1350, 47 USPQ2d 1453 (Fed. Cir. 1998). That an inventor achieved a claimed invention by doing what those skilled in the art suggested should not be done is a fact strongly probative of nonobviousness. *Kloster Speedsteel AB v. Crucible, Inc.,* 793 F.2d 1565, 230 USPQ 81 (Fed. Cir. 1986), *on rehearing,* 231 USPQ 160 (Fed. Cir. 1986). Further, even though a reference may be readily modified to form the claimed invention, the mere fact that the prior art can be so modified does not make the modification obvious unless the prior art suggests the desirability of the modification. *In re Laskowski,* 871 F.2d 115, 10 USPQ2d 1397 (Fed. Cir. 1989).

In the first Office Action on the merits, the Examiner rejected the claims as obvious over Sequeira et al. in view of the Maxair monograph. Sequeira et al. teaches the use of the corticosteroid mometasone for the treatment of upper and lower respiratory diseases and the Maxair monograph teaches the use of the short-acting bronchodilator pirbuterol for the treatment of asthma. Relying *In re Kerkhoven,* which holds that it is *prima facie* obvious to combine two compositions known to be useful for the same purpose, the Examiner asserted that the claimed invention is obvious.

In the Amendment filed on January 10, 2003, it was argued that the claimed invention is not rendered obvious by Sequeira et al. in view of the Maxair monograph because neither reference, alone or in combination, teaches or suggests a corticosteroid/short-acting bronchodilator combination *in a single formulation* (*see,* January 10, 2003, Amendment, p.6, 3rd full para.). Further it was noted that because corticosteroids and bronchodilators are not used for the same purpose within anti-asthma therapy, that *Kerkhoven* does not apply. In the Office Action under reply, the Examiner is maintaining the Sequeira et al. in view of the Maxair monograph rejection and is once again asserting that because a corticosteroid and a short-acting bronchodilator are both independently useful for the treatment of asthma and related illnesses, the administration of the two drugs in a single dosage form is an obvious modification. As set forth in the attached Kaplan Declaration, the Examiner's position does not take into consideration several critical aspects of the claimed invention, which are explained in detail *infra.*

The attached Kaplan Declaration addresses four critical aspects of the claimed invention that demonstrate its nonobviousness. These critical aspects are: (i) alleviation of the problems associated

with patient compliance of corticosteroid therapy; (ii) the superior effects of a short-acting bronchodilator/corticosteroid combination over a long-acting bronchodilator/corticosteroid combination; (iii) the improved compliance and effectiveness of corticosteroid therapy when a short-acting bronchodilator is administered simultaneously with a corticosteroid; and (iv) the addition of a short-acting bronchodilator to a corticosteroid in a single formulation goes against established principles in asthma therapy.

In the Kaplan Declaration, it is explained that patient compliance with corticosteroid therapy is a persistent problem resulting from the 24 to 72 hour delay in the onset of the corticosteroid effect (*see,* para. 9 of the Kaplan Declaration). Because patients do not detect any advantage to taking the corticosteroids within this critical time period, patients have a tendency to become noncompliant with their corticosteroid therapy. As will be explained below, the claimed combination alleviates the persistent problem of patient noncompliance that accompanies standard asthma therapy.

Attempts to relieve patients of the adverse effects of an asthma attack have included the addition of long-acting bronchodilators to corticosteroids, with the latter also being a long-acting medication (*see,* para. 10 of the Kaplan Declaration). One commercially available asthma medication that combines a corticosteroid (fluticasone propionate) with a long-acting bronchodilator (salmeterol) is the Advair® inhaler. Because the long-acting bronchodilator takes 30 to 45 minutes to exert any effect, a patient using the Advair inhaler must also carry a rescue inhaler housing a short-acting bronchodilator for immediate relief of asthma symptoms. Because self-administration of the short-acting bronchodilator will alleviate the asthma symptoms, the patient is left with little incentive to self-administer the Advair combination. This scenario demonstrates that both the addition of a long-acting bronchodilator to a corticosteroid and the use of a rescue inhaler housing a short-term bronchodilator fail to improve patient compliance with corticosteroid therapy.

A significant advantage of the claimed invention is that it alleviates the problems associated with patient compliance of corticosteroid therapy by administering corticosteroids along with short-term bronchodilators *in a single formulation.* With this combination, patients carry one inhaler that they use just like their rescue inhalers (which traditionally house only short-acting bronchodilators) and in so doing, also receive the benefits of their corticosteroid therapy (*see,* para. 11 of the Kaplan Declaration). In this way, the problem with patient compliance of corticosteroid therapy is completely alleviated.

Lastly, contrary to the Examiner's assertion that the claimed combination is obvious, a review of allergy therapeutics literature, and asthma treatment procedures in particular, demonstrates that combining a long-term corticosteroid with a short-acting bronchodilator has never been contemplated as an option by allergy specialists (*see,* para. 12 of the Kaplan Declaration, which references the *Guidelines*

for the Diagnosis and Management of Asthma, NIH Publication No. 97-4051 (July 1997), also attached). Because allergy medications are categorically separated according to their long-term and short-term effects, corticosteroids, which are long-term medications, and short-acting bronchodilators, which are short-term medications, have never been used together in a single combination. On this matter, applicants note that the Advair inhaler discussed *supra* combines a corticosteroid with a long-acting bronchodilator. In light of the established practices of allergy therapeutics, it follows that the claimed invention is one of those inventions that falls under the rubric expounded by the Federal Circuit in *Kloster Speedsteel*, that is, because the present invention goes against that which those skilled in the art suggest should not be done, the claimed invention is by its very nature, not obvious. *Kloster Speedsteel, supra*; *see also,* para. 13 of the Kaplan Declaration.

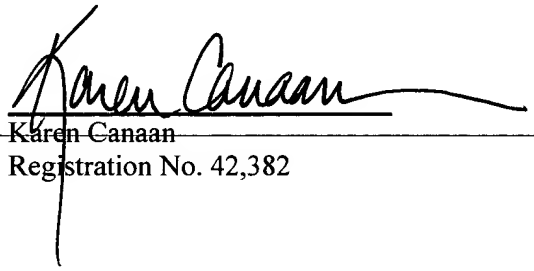
The foregoing analysis demonstrates unique aspects of the claimed invention that distinguish it from the teachings of Sequeira et al. and the Maxair monograph. Specifically, because there is no teaching in Sequeira et al. or the Maxair monograph to suggest the desirability of adding a short-acting bronchodilator to a long-term corticosteroid in *a single formulation*, it follows that Sequeira et al. in view of the Maxair inhaler provides no incentive for the ordinary artisan to modify the formulations disclosed therein so that the claimed invention is achieved. *See, In re Laskowski, supra.* Since the claimed invention is not rendered obvious by Sequeira et al. in view of the Maxair inhaler, applicants respectfully request reconsideration and withdrawal of this rejection.

CONCLUSION

The foregoing analysis shows that the obviousness rejection for this application should be reversed. Since the obviousness rejection discussed above is the only outstanding rejection for this case, upon reversal of the rejection, this application should be in condition for allowance.

If the Examiner has any additional issues with respect to this case that may be addressed by way of a personal communication with applicants' attorney, the Examiner is encouraged to contact the undersigned at 650-33-4913 or at canaan@reedpatent.com.

Respectfully submitted,

By: 

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